

Bioseparation Process Science

生物分离过程科学

Antonio A. García

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Bioseparation Process Science



PREFACE

In this textbook, the word *bioseparations* is used in the context of biochemical engineering. In this context, the term refers to separation and purification methods for such biological products as biochemicals, proteins, polynucleic acids, and cells. The purpose of this text is to provide students and practitioners of engineering and science with a framework for decision making in the design of bioseparation processes.

Chapter 1 introduces some of the basic concepts central to understanding the remainder of the book. Part I of the text then moves on to discuss some illustrative biotechnology industrial processes and provides the reader with practical information on standard analytical methods. The two chapters that constitute Part I are important bookends covering the full industrial and analytical scale of bio-separations. Chapter 2 covers a broad range of important industrial bioseparation processes, stressing an overview of the arrangement of individual steps in the purification of the final product. Chapter 3 provides a useful discussion of analytical methods, a topic too often ignored in biochemical engineering texts. Process evaluation, however, cannot be carried out without analytical support and analytical methods, which are often emulated and redesigned for commercial-scale production.

Part II touches on several challenging subject areas, describing physical, chemical, and biological interactions with an eye toward exploiting these effects for bioseparations. Physical and chemical interactions are normally covered in some depth in engineering textbooks, and biological interactions are the focus of biochemistry texts. Within this section of the book, we present these different views simultaneously so as to give the student and the practitioner a more complete set of tools with which to design purification and separation processes.

Part III deals with commonly employed “unit” operations (that is, process steps). Its organization parallels the format used in many biochemical engineering textbooks, though we have made an effort to keep the number of symbols and parameters to a minimum so as to focus on the phenomena themselves. In addition, the use of differential calculus is primarily confined to standard first- and second-semester calculus topics, with the exception of the use of Laplace transforms (an orientation to Laplace transforms is provided in the appendices). Our goal in reducing the number of symbols and the level of math complexity is to lower the barriers erected by the use of excessive mathematical jargon and specialized techniques in the multidisciplinary environment of industrial biotechnology. Readers interested in more mathematical content are encouraged to review the specialized textbooks and references cited throughout this book.

Part IV, the final section of the text, covers several key topics necessary to begin the creative process of synthesizing a biological separation process flow diagram. One of the most important tools for designing such processes is computer software, which provides a built-in wealth of expert information. Part IV acknowledges the efficiency and effectiveness of using these tools by *not* subjecting the reader to pencil-and-paper methods that serve only to reinvent the capabilities of currently

available software. Once the underlying principles and individual operation analyses of Parts II and III are covered, the practicing bioseparation process designer can learn to use the software design tools presented in Part IV, gaining an understanding of the underlying economics, process integration challenges, and final product formulation issues affecting bioseparations in the real world.

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CONTENTS

Preface	xv
1. Introduction	1
1.1 Mass Conservation as an Accounting Method	1
1.2 Interpreting Differentials and Integrals: World Population Statistics	3
1.3 Accounting for Diffusion, Convection, and Reaction for Mass Conservation: The Microscopic Scale	5
1.4 Summary	7
1.5 References	7
Part I. Commercial Bioseparations and Product Measurement	9
2. Industrial Bioseparation Processes	11
2.1 Bioseparation Process Selection	11
2.1.1 Scale, Concentration, and Price	13
2.1.2 Product Properties	14
2.2 Monoclonal Antibodies	16
2.3 Human Insulin	17
2.4 Rabies Vaccine	17
2.5 Penicillin	19
2.6 Protease	20
2.7 L-lysine	21
2.8 Citric Acid	22
2.9 Summary	23
2.10 Problems	24
2.11 References	28
3. Concentration Determination and Bioactivity Assays	29
3.1 Amino Acids	29
3.1.1 High-Performance Liquid Chromatography	31
3.1.2 Reverse-Phase High-Performance Liquid Chromatography	32
3.1.3 Capillary Electrophoresis	32
3.1.4 Micellar Electrokinetic Chromatography	33
3.1.5 Electrodialysis	34
3.1.6 Gas Chromatography	35
3.2 Peptides and Proteins	35
3.2.1 Analytical Chromatography	35
3.2.2 Analytical Electrophoresis	37
3.2.3 Immunoassays	40

3.3	Nucleic and Polynucleic Acids	41
3.3.1	Ion-Exchange Chromatography	41
3.3.2	Reverse-Phase High-Performance Liquid Chromatography	42
3.3.3	Ion-Pair Chromatography	43
3.3.4	Slalom Chromatography	43
3.3.5	Gel Electrophoresis	44
3.3.6	Pulsed-Field Gel Electrophoresis	45
3.3.7	Capillary Isotachophoresis	45
3.3.8	Capillary Zone Electrophoresis	45
3.4	Carbohydrates	46
3.4.1	Monosaccharides	46
3.4.2	Oligosaccharides	49
3.4.3	Glycoproteins	51
3.5	Lipids	51
3.5.1	Fatty Acids	51
3.5.2	Fats and Oils	56
3.6	Steroids and Antibiotics	56
3.7	Vitamins	57
3.8	Summary	58
3.9	Problems	59
3.10	References	61
 Part II. Application of Chemical, Physical, and Biological Properties to Bioseparations		65
4.	Thermodynamic and Transport Properties	67
4.1	Chemical Equilibria	67
4.2	Solubility	69
4.2.1	Protein and Amino Acid Solubility	70
4.3	Diffusivity	73
4.3.1	Uncharged Low-Molecular-Weight Biochemicals	73
4.3.2	Proteins	73
4.4	Isoelectric Points and Charge Dependence on pH	74
4.4.1	Carboxylic Acids	74
4.4.2	Amino Acids	76
4.4.3	Proteins	82
4.5	Hydrophobicity–Hydrophilicity Scales	84
4.6	Acid-Base Scales	84
4.6.1	Gutmann Donor-Acceptor Theory	84
4.6.2	Drago E&C Equation	86

4.6.3	Solvatochromatic Comparison Method	86
4.6.4	Hard and Soft Acid and Base Theory	86
4.6.5	Comparison and Correlation of Different Scales	88
4.7	Metal Ion Binding Constants	88
4.7.1	Nucleic Acids	89
4.7.2	Amino Acids	89
4.8	Summary	90
4.9	Problems	91
4.10	References	93
5.	Biocolloidal Interactions and Forces	95
5.1	Short-Range Interactions	95
5.2	Long-Range Interactions	96
5.2.1	Van der Waals Forces	96
5.2.2	Electrostatic Interactions and DLVO Theory	100
5.2.3	Hydrophobic Effects	102
5.2.4	Magnetic Interactions	103
5.3	Summary	104
5.4	Problems	105
5.5	References	106
6.	Bioaffinity	108
6.1	Molecular Recognition Processes	108
6.2	Receptor-Ligand Interactions	110
6.2.1	Ionic Bonds	110
6.2.2	Hydrogen Bonds	110
6.2.3	Hydrophobic Interactions	111
6.2.4	Van der Waals Forces	111
6.3	Theoretical Aspects of Receptor-Ligand Affinity	111
6.3.1	Thermodynamic Approach	112
6.3.2	Equilibrium Approach	112
6.4	Specific Interactions	115
6.4.1	Antibody-Antigen Interactions	116
6.4.2	DNA-Protein Interactions	117
6.4.3	Cell Receptor-Ligand Interactions	119
6.4.4	Enzyme-Substrate Interactions	120
6.4.5	Biotin-Avidin/Streptavidin Interactions	121
6.4.6	Lectin-Carbohydrate Interactions	122
6.5	Summary	122
6.6	Problems	123
6.7	References	124

Part III. Bioseparation Methods	125
7. Crystallization and Precipitation	127
7.1 Saturation and Supersaturation	127
7.2 Nucleation Phenomena	128
7.3 Growth of Crystals	130
7.4 Batch Crystallization	131
7.4.1 Solution Balance	132
7.4.2 Solid-Phase Balance	132
7.4.3 Crystal Size Distribution	134
7.4.4 Organic Solvent and Salt Precipitation	136
7.4.5 Growth Rate Dispersion	137
7.5 Continuous Crystallization	140
7.6 Yield	141
7.6.1 Removal of Solvent and Diluent	141
7.7 Summary	142
7.8 Problems	142
7.9 References	145
8. Membrane Filtration	146
8.1 Membrane Materials	146
8.2 Driving Forces in Membrane Separations	147
8.3 General Theory of Microfiltration	147
8.3.1 Incompressible Cakes	148
8.3.2 Compressible Cakes	149
8.4 Microfiltration	149
8.4.1 Staging in Microfiltration	151
8.5 Ultrafiltration	152
8.5.1 Ultrafiltration Process Application	154
8.5.2 Ultrafiltration Membrane Application and Modification	156
8.6 Reverse Osmosis	156
8.7 Flux Equations	158
8.8 Electrodialysis	158
8.9 Emulsion Liquid Membranes	159
8.10 Summary	160
8.11 Problems	160
8.12 References	163
9. Centrifugation	164
9.1 Governing Principles	164
9.2 Advantages and Disadvantages of Centrifugation	166

9.3	Selection of Centrifuges	166
9.4	Types of Centrifuges	168
9.4.1	Tubular Bowl Centrifuges	169
9.4.2	Disc-Type Centrifuges	170
9.4.3	Batch-Basket Centrifuges	172
9.5	Industrial-Scale Centrifugation	173
9.6	Summary	176
9.7	Problems	176
9.8	References	177
10.	Chromatography	178
10.1	Detection Methods	178
10.2	Summary of the Types of Chromatography	181
10.3	Stationary Phases	183
10.4	Six Ways to Analyze Chromatographic Processes	187
10.4.1	Gaussian Solution	187
10.4.2	Staged Models	190
10.4.3	Newtonian Continuum Mechanics and Linear Equilibria	196
10.4.4	Constant Pattern and Saturation Equilibria	200
10.4.5	Van Deemter Equation	205
10.4.6	Gel Partitioning Model	205
10.5	Gel-Permeation Chromatography	206
10.6	Ion-Exchange Chromatography	208
10.7	Affinity Chromatography	213
10.8	Hydrophobic Interaction and Reverse-Phase Chromatography	216
10.9	Perfusion Chromatography	216
10.10	Other Chromatographic Methods	217
10.10.1	Gradient Methods	217
10.10.2	Displacement Chromatography	218
10.10.3	Radial-Flow Chromatography	218
10.10.4	Membrane Chromatography	218
10.11	Scale-Up Strategies and Considerations	219
10.11.1	Scale-Up Method 1: No Change in Stationary- Phase Particle Size	220
10.11.2	Scale-Up Method 2: Increasing Stationary-Phase Particle Size	221
10.11.3	Scale-Up Method 3: Gel Permeation and On-Off Cycling Approach	222

10.12 Summary	223
10.13 Problems	224
10.14 References	228
11. Extraction	230
11.1 Chemical Thermodynamics of Partitioning	230
11.2 Organic-Aqueous Extraction	231
11.2.1 Extractant/Diluent Systems	233
11.2.2 Removing Biochemicals from the Organic Phase	237
11.3 Two-Phase Aqueous Extraction	238
11.3.1 Partitioning Due to Size	239
11.3.2 The Effect of Protein Charge on Partitioning	240
11.3.3 Other Effects	241
11.4 Reverse Micelles	243
11.5 Supercritical Fluids	244
11.6 Large-Scale Vessels for Extraction	246
11.6.1 Mixer-Settlers	246
11.6.2 Extraction Columns	247
11.6.3 Centrifugal Contactors	250
11.6.4 Comparison	251
11.7 Configurations for Stage-Wise Contacting	252
11.7.1 Cocurrent Contacting	252
11.7.2 Crosscurrent Contacting	253
11.7.3 Countercurrent Contacting	254
11.7.4 A Comparison of Contacting Modes	255
11.7.5 Graphical Solution	263
11.7.6 Fractional Extraction	265
11.7.7 Continuous Countercurrent Extraction	269
11.8 Summary	270
11.9 Problems	271
11.10 References	276
12. Electrophoresis	277
12.1 A Brief Introduction to Some Popular Electrophoretic Methods	277
12.1.1 Gel Electrophoresis	278
12.1.2 Capillary Electrophoresis	281
12.1.3 Isoelectric Focusing	282
12.1.4 Isotachophoresis	283
12.1.5 Moving Boundary	283
12.2 Basic Concepts of Electrophoresis	283

12.2.1	Electro-osmosis and the Relaxation Effect as Retardation Forces	286
12.2.2	Situations That Can Hamper Electrophoretic Separation	286
12.3	Zone Electrophoresis	287
12.3.1	Band Dispersion	288
12.4	Isoelectric Focusing	290
12.5	Isotachopheresis	291
12.6	Two-Dimensional Electrophoresis	292
12.7	Summary	294
12.8	Problems	294
12.9	References	298
13.	Magnetic Bioseparations	299
13.1	Magnetic Properties of Materials	299
13.2	Magnetic Particle Classification	305
13.3	Theoretical Considerations	306
13.4	Magnetic Particle Separations	308
13.4.1	High-Gradient Magnetic Separations	309
13.4.2	Affinity Chromatography	310
13.4.3	Aqueous Two-Phase Separations	311
13.5	Applications	312
13.5.1	Cell Separation	312
13.5.2	Immunoassays	313
13.6	Summary	313
13.7	Problems	313
13.8	References	314
14.	Solvent Removal and Drying	315
14.1	Methods of Solvent Removal	315
14.2	Theory	316
14.2.1	Vapor-Liquid Systems	317
14.2.2	Liquid-Liquid Systems	321
14.2.3	Liquid-Solid Systems	323
14.3	Rayleigh Distillation	325
14.4	Equipment	327
14.4.1	Evaporation	327
14.4.2	Drying	331
14.5	Summary	334
14.6	Problems	334
14.7	References	336

15. Cell Disruption	337
15.1 Cells and Cell Membranes	337
15.2 Cell Disruption Techniques	339
15.2.1 Mechanical Cell Disruption	340
15.2.2 Chemical Cell Disruption	348
15.3 Summary	350
15.4 Problems	351
15.5 References	352
Part IV. Bioprocess Synthesis	355
16. Integration of Individual Separation Steps	357
16.1 Bioseparation Process Heuristics	357
16.1.1 Reduce Volume Early in the Process Sequence	358
16.1.2 Save the Most Expensive Step for Last	358
16.1.3 Follow the KISS Principle	360
16.1.4 Resolve Components Well as Early as Possible	361
16.1.5 Minimize Inhibition Mechanisms in the Bioreactor	362
16.2 Issues in Concurrent Bioseparation and Bioreactor Process Development	362
16.2.1 Take the Lab-Scale Process and Scale It Directly with No Changes	362
16.2.2 Design a Bioseparation Process Based on the Closest Existing Commercial Product	363
16.2.3 Pilot-Scale Experimentation with “Spiked” Bioreactor Fluid	363
16.3 Expert Systems in Process Synthesis	364
16.4 Integration of Bioreaction and Bioseparation Steps	364
16.5 Making the Bioreactor Step Bioseparation-Friendly	366
16.6 Considerations in Final Product Formulation and Environmental Impact	367
16.7 Summary	368
16.8 Problems	369
16.9 References	371
17. Production Formulation	372
17.1 Formulation Characteristics	372
17.2 Excipients	373
17.2.1 Thickeners and Binders	373
17.2.2 Surface-Active Agents	374
17.2.3 Colors and Flavors	374
17.2.4 Preservatives	374

17.3	Dosage Forms	375
17.4	Encapsulation	375
17.5	Freeze Drying	377
17.5.1	Theory	378
17.5.2	Technique	381
17.6	Summary	383
17.7	Problems	383
17.8	References	383
18.	Bioprocess Economics	385
18.1	Resources Available for Cost Estimation	385
18.1.1	Capital Cost Estimation	386
18.1.2	Operating Cost Estimation	388
18.2	Economic Decision-Making Models	389
18.2.1	Internal Rate of Return	391
18.2.2	Payback Period, Including Interest	391
18.2.3	Net Present Value	391
18.2.4	Return on Investment	392
18.2.5	Choosing Among Projects and Alternative Investments	394
18.3	Sensitivity Analyses	394
18.4	Summary	398
18.5	Problems	398
18.6	References	399
Appendix A. The Laplace Transform		400
Appendix B. Numerical Inversion, van der Laan's Theorem, and Huchel and Helmholtz-Smoluchowski Equations		405
Index		409

Introduction

Throughout this textbook, the reader will encounter the application of calculus, which is usually associated with the principle of conservation of mass. Traditionally, the use of calculus in textbooks signals that the book is directed toward readers who are studying engineering or who have an engineering background. The approach taken in this book, however, will be to apply useful mathematics to the analysis of bioseparation processes in such a way as to permit access by a wider scientific audience. Both this introductory chapter and Appendix A are designed to help bridge the so-called engineering–mathematics gap—that is, to make the coverage of these topics suitable for a reader who has completed one semester of calculus and physics. Moreover, we have kept the number of defined terms to a minimum whenever possible, and avoided the use of intricate mathematical methods so as to present a uniform and straightforward use of analysis tools.

This chapter deals with three analysis tools applicable to bioseparation processes:

- The principle of mass conservation as an accounting method
- The use of differentials and integrals to help answer important questions
- Chemical species accounting for processes involving diffusion, convection, or reaction

Appendix A introduces the use of Laplace transforms as a convenient method for solving the differential equations with which we model separation processes. The reader can skip this chapter if desired, returning to it as questions arise on the use of mathematics in our subsequent discussions of chromatography, solvent extraction, and crystallization.

1.1 MASS CONSERVATION AS AN ACCOUNTING METHOD

Science students will be familiar with the oft-quoted law of classical physics that states that “mass is neither created nor destroyed.” This statement of mass conservation holds unless a nuclear reaction occurs, in which case Einstein’s equation relating mass to energy must then be employed. For the purpose of bioseparations, this law holds true in every situation. Thus, in bioseparation process science, the law of mass conservation provides a basis for writing mathematical expressions to help predict the outcome for design variables based on the nature of the process.

The application of the law of mass conservation is entirely analogous to financial accounting or any other type of accounting. An anecdote will illustrate how to perform such mass accounting. Imagine that a professor brings a closed cardboard

box and a basket of balls into class. She then requests that a student come to the front of the room to help in adding and removing balls to and from the box. The professor opens the box and allows the student to start by adding eight balls. Then she has him remove two balls. The rest of the class is charged with keeping track of the number of balls being added to and removed from the box.

After several rounds of adding or removing balls from the box, the professor asks the class how many balls are in the box. Nearly everyone in the room answers the professor in unison. The professor, however, tells them that they are all wrong. After checking their tallies, the class members are even more firmly convinced that they have the right number. Yet the professor still claims that they are wrong. Finally, the class has become thoroughly incensed and accuses the professor of not being able to count. “Of course, you have the wrong answer,” she exclaims. One student asks, “How can that be? We carefully tracked the number of balls that were added and subtracted, and then double-checked our answer.” “But,” says the professor, “you did not know that there were four balls in the box when I brought it into class.”

This anecdote illustrates the importance of carefully and explicitly constructing an accounting procedure for mass. The proper way of dealing with accounting for the number of balls in the box at any time is to write a procedure, such as the following:

$$\left[\begin{array}{c} \text{Number of} \\ \text{balls in box} \\ \text{at any time} \end{array} \right] = \left[\begin{array}{c} \text{number of} \\ \text{balls in box} \\ \text{initially } (t = 0) \end{array} \right] + \left[\begin{array}{c} \text{number of balls} \\ \text{added since the} \\ \text{beginning } (t > 0) \end{array} \right] - \left[\begin{array}{c} \text{number of balls} \\ \text{removed since the} \\ \text{beginning } (t > 0) \end{array} \right] \quad (1.1)$$

A mathematical equation can be created from Equation 1.1 when $b(t)$ is defined as the number of balls in the box at any time, $b(0)$ is the number of balls in the box initially, b_{in} is the number of balls put into the box, and b_{out} is the number of balls removed from the box. After substituting these expressions into Equation 1.1, we have the following equation:

$$b(t) = b(0) + b_{\text{in}} - b_{\text{out}} \quad (1.2)$$

In most cases, it is more useful to track rates than absolute numbers. For example, a person may want to know how fast his net worth is changing over time. This rate is especially important if the person wants to see whether bankruptcy is imminent or whether he is saving enough for retirement. In that case, one equation could satisfy this need:

$$\left[\begin{array}{c} \text{Rate of accumulation} \\ \text{of dollars (\$/month)} \end{array} \right] = \left[\begin{array}{c} \text{salary rate after} \\ \text{taxes (\$/month)} \end{array} \right] + \left[\begin{array}{c} \text{net rate of cash flow due} \\ \text{to investments (\$/month)} \end{array} \right] - \left[\begin{array}{c} \text{expense rate} \\ \text{(\$/month)} \end{array} \right] \quad (1.3)$$

For our simpler box problem, we can also change the accounting method to a rate:

$$\left[\begin{array}{c} \text{Rate of accumulation} \\ \text{of balls (\#/minute)} \end{array} \right] = \left[\begin{array}{c} \text{rate of balls into} \\ \text{box (\#/minute)} \end{array} \right] - \left[\begin{array}{c} \text{rate of balls out of} \\ \text{box (\#/minute)} \end{array} \right] \quad (1.4)$$